



PATENT  
Docket No. 368292000200

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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In the application of:

Philip J. BARR, et al.

Serial No.: 10/025,514

Filing Date: December 18, 2001

For: MULTIFUNCTIONAL PROTEASE  
INHIBITORS AND THEIR USE IN  
TREATMENT OF DISEASE

Examiner: M. Walicka

Group Art Unit: 1652

TECH CENTER 1600/2900

RESPONSE TO RESTRICTION REQUIREMENT

Assistant Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

This is in response to the Office Action dated July 23, 2002, (Paper No. 9) for which a response was due on August 23, 2002 and for which a 1 month extension of time is also requested to extend the time for response from August 23, 2002 to September 23, 2002.

The Examiner requires restriction to one of the following inventions:

I. Claims 2, 4, 8 in part, 11, 16, 17, drawn to a fusion protein comprising a first protease inhibitor comprising alpha 1- antitrypsin, or a functionally active portion thereof, and a second protease inhibitor that is a secretory leukocyte protease inhibitor, or a functionally active portion thereof classified in class 435, subclass 69.2.

II. Claim 3, 8 in part, 12, 15, 18, 19, 20, drawn to a fusion protein comprising a first protease inhibitor comprising alpha 1- antitrypsin or a functionally active portion thereof and a second protease inhibitor that is a tissue inhibitor of metalloprotease, or a functionally active portion thereof (amino acids 1-107), classified in class 435, subclass 69.2.

III. Claim 3, 8 in part, 12, 21, 22, 23, drawn to a fusion protein comprising a first protease inhibitor comprising alpha 1- antitrypsin or a functionally active portion thereof, and a second protease inhibitor that is a tissue inhibitor of metalloprotease, or a functionally active portion thereof (amino acids 1-184), classified in class 435, subclass 69.2.

IV. Claim 3, 8 in part, 12, 21, 22, 23, drawn to a fusion protein comprising a first protease inhibitor comprising alpha 1- antitrypsin or a functionally active portion thereof, and a functionally active portion of a tissue inhibitor of metalloprotease, (S-linked TAPI), classified in class 435, subclass 69.2.

V. Claims 1 and 13 drawn to a fusion protein comprising a first protease inhibitor comprising alpha 1- antitrypsin, or a functionally active portion thereof, and a second protease inhibitor that inhibits an aspartyl protease, classified in class 435, subclass 69.2.

VI. Claims 1 and 14 drawn to a fusion protein comprising a first protease inhibitor comprising alpha 1- antitrypsin, or a functionally active portion thereof, and a second protease inhibitor that inhibits a cysteine protease, classified in class 435, subclass 69.2.

VII. Claims 5, 6, 7, 9, and 10, drawn to a polynucleotide encoding the fusion protein of claim 1, expression vector, host cell comprising said vector, recombinant method of production the fusion protein, classified in class 435, subclass 69.7.

VIII. Claim 26-28, drawn to a method for inhibiting protease activity, classified in class 435, subclass 23.

IX. Claim 29-35, drawn to a method of treating an individual comprising administering to the individual an effective amount of the fusion protein classified in class 514, subclass 12.

In addition, inventions VII, VIII and IX above are generic to a plurality of disclosed patentably distinct species comprising:

- (A). fusion protein of claim 1.
- (B). fusion protein of claim 2.
- (C). fusion protein of claim 3.
- (D). fusion protein of claim 4.

Applicants traverse this restriction requirement and respectfully request reconsideration based upon the following comments.

As an initial matter, Applicants note that Groups I-VI have been classified by the Examiner as belonging to class 435, subclass 69.2. Applicants respectfully point out that no search burden is indicated based on this same classification/subclassification scheme. Because no burden of search is present in searching a single subclass (in contrast to the requirement for a "serious burden" at MPEP §803), the reasons for restriction between these Groups are insufficient and the restriction may be properly withdrawn.

Applicants respectfully request withdrawal of the restriction among Groups II, III, and IV. Groups II, III, and IV<sup>1</sup> are joined by a linking claim and, furthermore, represent a combination/subcombination grouping.

Claim 12, present in each of Groups II, III, and IV, is a linking claim for claims 3, 15, 18, and 19 of Group II, claims 3, 21, 22, and 23 of Group III, and claims 3, 12, 24 and 25 of Group IV. Claim 12 is to a fusion protein comprising a first protease inhibitor comprising alpha one-antitrypsin or a functionally active portion thereof and a second protease inhibitor or functionally active portion thereof, where the second protease inhibits a metalloprotease. Claims 3, 15, 18, 19, and 21-25 are all drawn to species within the genus claimed by claim 12; therefore, claim 12

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<sup>1</sup> It appears that there is a typographical error and that Group IV should read "claims 3, 8 in part, 12, 24 and 25," which is the group corresponding to the S-linked TAPI, the embodiment that the Examiner states is the basis of Group IV, rather than "claims 3, 8 in part, 12, 21, 22, and 23," which is how it reads in the Office Action, and which is an exact duplicate of Group III.

is a linking claim. If claim 12 is deemed a linking claim and is found allowable, all linked inventions must be examined. See MPEP §809.03.

In addition, Groups III and IV and Group II are related as sub-combination / combination and as such the USPTO is obligated to follow its own rules. See MPEP §806.05. There is no search burden placed upon the Examiner in searching the claims of Group II and Groups III and IV together because the sub-combinations, that is Groups III and IV, must be searched as part of the combination, that is, Group II. All of the claims in Groups II, III, and IV are drawn to fusion proteins comprising amino acids from about 1 to about 394 of alpha 1-antitrypsin (AAT), linked to tissue inhibitor of metalloproteases-1 (TIMP-1), in whole or in part. There is no additional burden placed on the Examiner to search amino acids from about 1 to about 394 of AAT linked to amino acids about 1 to about 184 of TIMP-1 (Group II) as compared to amino acids about 1 to about 126 of TIMP-1 (Group III) or amino acids about 1 to about 127 of TIMP-1 (Group IV). In fact, the Examiner places them in the same class and subclass (class 435, subclass 69.2.). The difference between groups III and IV is only one amino acid from the same sequence. Therefore, restriction of these claims may be properly withdrawn, and Applicants request that Groups II, III, and IV be rejoined for examination.

Applicants hereby elect Group I, with traverse. Because election of species was required only if Group VII, VIII or IX was elected, Applicants have not elected a species.

Applicants note that claim 1 should be joined to the present claims for Group I.<sup>2</sup> Claim 1, which is drawn to a fusion protein of alpha one-antitrypsin or a functionally active portion thereof joined to a second protease inhibitor or functionally active portion thereof, is already part of Group V (wherein the second protease inhibitor inhibits an aspartyl protease, claim 13) and Group VI (wherein the second protease inhibitor inhibits a cysteinyl protease, claim 14). Likewise, claim 1 should also be included in Group I (wherein the second protease inhibitor

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<sup>2</sup> Similarly, claim 1 should be included in groups II-IV. Claim 1 is a linking claim for these groups, because claim 1 is to a genus of which claims in each of Groups I-VI are species. If claim 1 is deemed a linking claim and is found allowable, all linked inventions must be examined. See MPEP §809.03.

inhibits a serine protease, claim 11). Applicants respectfully request that claim 1 be joined to Group I for examination. Applicants understand that, in examining Group I, the search will initially focus on the components of the fusion protein of this group as described in the Office Action.

Applicants also respectfully point out that the claims of Groups VIII and IX are methods claims that incorporate all of the limitations of composition claims contained in Group I (i.e., claims 2 and 4, and claim 1 if it is joined). Thus, should the Examiner find any of these claims allowable, rejoinder of amended claims of Groups VIII and IX is proper and Applicants will at that time request rejoinder of methods claims of Groups VIII and IX to the extent they incorporate all the limitations of allowed composition claims, of Groups I-VI. *In re Ochiai*.

Applicants expressly reserve their right under 35 U.S.C. § 121 to file a divisional application directed to the nonelected subject matter during the pendency of this application, or an application claiming priority from this application.

Applicants request examination of the elected subject matter on the merits.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 368292000200. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: September 20, 2002

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